Human Secreted Proteins

[1] This application is a continuation-in-part of, and claims benefit under 35 U.S.C. § 119(e) based on copending U.S. Provisional Application No. 60/278,650 filed on March 27, 2001. This application is also a continuation-in-part of, and claims benefit under 35 U.S.C. § 120 of copending U.S. Utility Application No. 09/833,245, filed on April 12, 2001, and PCT International Application Serial No. US01/11988, filed on April 12, 2001. This application is also a continuation-in-part of, and claims benefit under 35 U.S.C. § 120 of copending PCT International Application Serial No. US00/06043, filed on March 9, 2000, which claims benefit under 35 U.S.C. § 119(e) based on U.S. Provisional Application No. 60/167,061, filed on November 23, 1999, and U.S. Provisional Application No. 60/124,146, filed on March 12, 1999. This application is also a continuation-in-part of, and claims benefit under 35 U.S.C. § 120 of copending PCT International Application Serial No. US00/06012, filed on March 9, 2000, which claims benefit under 35 U.S.C. § 119(e) based on U.S. Provisional Application No. 60/166,989, filed on November 23, 1999, and U.S. Provisional Application No. 60/124,093, filed on March 12, 1999. This application is also a continuation-in-part of, and claims benefit under 35 U.S.C. § 120 of copending PCT International Application Serial No. US00/06058, filed on March 9, 2000, which claims benefit under 35 U.S.C. § 119(e) based on U.S. Provisional Application No. 60/168,654, filed on December 3, 1999, and U.S. Provisional Application No. 60/124,145, filed on March 12, 1999. This application is also a continuation-in-part of, and claims benefit under 35 U.S.C. § 120 of copending PCT International Application Serial No. US00/06044, filed on March 9, 2000, which claims benefit under 35 U.S.C. § 119(e) based on U.S. Provisional Application No. 60/168,661, filed on December 3, 1999, and U.S. Provisional Application No. 60/124,099, filed on March 12, 1999. This application is also a continuation-in-part of, and claims benefit under 35 U.S.C. § 120 of copending PCT International Application Serial No. US00/06059, filed on March 9, 2000, which claims benefit under 35 U.S.C. § 119(e) based on U.S. Provisional Application No. 60/168,622, filed on December 3, 1999, and U.S. Provisional Application No. 60/124,096, filed on March 12, 1999. This application

is also a continuation-in-part of, and claims benefit under 35 U.S.C. § 120 of copending PCT International Application Serial No. US00/06042, filed on March 9, 2000, which claims benefit under 35 U.S.C. § 119(e) based on U.S. Provisional Application No. 60/168,663, filed on December 3, 1999, and U.S. Provisional Application No. 60/124,143, filed on March 12, 1999. This application is also a continuation-in-part of, and claims benefit under 35 U.S.C. § 120 of copending PCT International Application Serial No. US00/06014, filed on March 9, 2000, which claims benefit under 35 U.S.C. § 119(e) based on U.S. Provisional Application No. 60/168,665, filed on December 3, 1999, and U.S. Provisional Application No. 60/138,598, filed on June 11, 1999, and U.S. Provisional Application No. 60/124,095, filed on March 12, 1999. This application is also a continuation-in-part of, and claims benefit under 35 U.S.C. § 120 of copending PCT International Application Serial No. US00/06013, filed on March 9, 2000, which claims benefit under 35 U.S.C. § 119(e) based on U.S. Provisional Application No. 60/168,662, filed on December 3, 1999, and U.S. Provisional Application No. 60/138,626, filed on June 11,1999, and U.S. Provisional Application No. 60/125,360, filed on March 19, 1999. This application is also a continuation-in-part of, and claims benefit under 35 U.S.C. § 120 of copending PCT International Application Serial No. US00/06049, filed on March 9, 2000, which claims benefit under 35 U.S.C. § 119(e) based on U.S. Provisional Application No. 60/168,667, filed on December 3, 1999, and U.S. Provisional Application No. 60/138,574, filed on June 11, 1999, and U.S. Provisional Application No. 60/124,144, filed on March 12, 1999. This application is also a continuation-in-part of, and claims benefit under 35 U.S.C. § 120 of copending PCT International Application Serial No. US00/06057, filed on March 9, 2000, which claims benefit under 35 U.S.C. § 119(e) based on U.S. Provisional Application No. 60/168,666, filed on December 3, 1999, and U.S. Provisional Application No. 60/138,597, filed on June 11, 1999, and U.S. Provisional Application No. 60/124,142, filed on March 12, 1999. This application is also a continuation-in-part of, and claims benefit under 35 U.S.C. § 120 of copending PCT International Application Serial No. US00/06824, filed on March 16, 2000, which claims benefit under 35 U.S.C. § 119(e) based on U.S. Provisional Application No. 60/168,664, filed on December 3, 1999, and U.S. Provisional Application No. 60/125,359, filed on March 19, 1999. This application is also a continuation-in-part of, and claims benefit under 35 U.S.C. § 120 of copending PCT International Application Serial No. US00/06765, filed on March 16, 2000, which claims benefit under 35 U.S.C. § 119(e) based on U.S. Provisional Application No. 60/169,906, filed on December 10, 1999, and

U.S. Provisional Application No. 60/126,051, filed on March 23, 1999. This application is also a continuation-in-part of, and claims benefit under 35 U.S.C. § 120 of copending PCT International Application Serial No. US00/06792, filed on March 16, 2000, which claims benefit under 35 U.S.C. § 119(e) based on U.S. Provisional Application No. 60/169,980, filed on December 10, 1999, and U.S. Provisional Application No. 60/125,362, filed on March 19, 1999. This application is also a continuation-in-part of, and claims benefit under 35 U.S.C. § 120 of copending PCT International Application Serial No. US00/06830, filed on March 16, 2000, which claims benefit under 35 U.S.C. § 119(e) based on U.S. Provisional Application No. 60/169,910, filed on December 10, 1999, and U.S. Provisional Application No. 60/125,361, filed on March 19, 1999. This application is also a continuation-in-part of, and claims benefit under 35 U.S.C. § 120 of copending PCT International Application Serial No. US00/06782, filed on March 16, 2000, which claims benefit under 35 U.S.C. § 119(e) based on U.S. Provisional Application No. 60/169,936, filed on December 10, 1999, and U.S. Provisional Application No. 60/125,812, filed on March 23, 1999. This application is also a continuation-in-part of, and claims benefit under 35 U.S.C. § 120 of copending PCT International Application Serial No. US00/06822, filed on March 16, 2000, which claims benefit under 35 U.S.C. § 119(e) based on U.S. Provisional Application No. 60/169,916, filed on December 10, 1999, and U.S. Provisional Application No. 60/126,054, filed on March 23, 1999. This application is also a continuation-in-part of, and claims benefit under 35 U.S.C. § 120 of copending PCT International Application Serial No. US00/06791, filed on March 16, 2000, which claims benefit under 35 U.S.C. § 119(e) based on U.S. Provisional Application No. 60/169,946, filed on December 10, 1999, and U.S. Provisional Application No. 60/125,815, filed on March 23, 1999. This application is also a continuation-in-part of, and claims benefit under 35 U.S.C. § 120 of copending PCT International Application Serial No. US00/06828, filed on March 16, 2000, which claims benefit under 35 U.S.C. § 119(e) based on U.S. Provisional Application No. 60/169,616, filed on December 8, 1999, and U.S. Provisional Application No. 60/125,358, filed on March 19, 1999. This application is also a continuation-in-part of, and claims benefit under 35 U.S.C. § 120 of copending PCT International Application Serial No. US00/06823, filed on March 16, 2000, which claims benefit under 35 U.S.C. § 119(e) based on U.S. Provisional Application No. 60/169,623, filed on December 8, 1999, and U.S. Provisional Application No. 60/125,364, filed on March 19, 1999. This application is also a continuation-in-part of, and claims benefit under 35 U.S.C. § 120 of copending

PCT International Application Serial No. US00/06781, filed on March 16, 2000, which claims benefit under 35 U.S.C. § 119(e) based on U.S. Provisional Application No. 60/169,617, filed on December 8, 1999, and U.S. Provisional Application No. 60/125,363, filed on March 19, 1999. This application is also a continuation-in-part of, and claims benefit under 35 U.S.C. § 120 of copending PCT International Application Serial No. US00/07505, filed on March 22, 2000, which claims benefit under 35 U.S.C. § 119(e) based on U.S. Provisional Application No. 60/172,410, filed on December 17, 1999, and U.S. Provisional Application No. 60/126,502, filed on March 26, 1999. This application is also a continuation-in-part of, and claims benefit under 35 U.S.C. § 120 of copending PCT International Application Serial No. US00/07440, filed on March 22, 2000, which claims benefit under 35 U.S.C. § 119(e) based on U.S. Provisional Application No. 60/172,409, filed on December 17, 1999, and U.S. Provisional Application No. 60/126,503, filed on March 26, 1999. This application is also a continuation-in-part of, and claims benefit under 35 U.S.C. § 120 of copending PCT International Application Serial No. US00/07506, filed on March 22, 2000, which claims benefit under 35 U.S.C. § 119(e) based on U.S. Provisional Application No. 60/172,412, filed on December 17, 1999, and U.S. Provisional Application No. 60/126,505, filed on March 26, 1999. This application is also a continuation-in-part of, and claims benefit under 35 U.S.C. § 120 of copending PCT International Application Serial No. US00/07507, filed on March 22, 2000, which claims benefit under 35 U.S.C. § 119(e) based on U.S. Provisional Application No. 60/172,408, filed on December 17, 1999, and U.S. Provisional Application No. 60/126,594, filed on March 26, 1999. This application is also a continuation-in-part of, and claims benefit under 35 U.S.C. § 120 of copending PCT International Application Serial No. US00/07535, filed on March 22, 2000, which claims benefit under 35 U.S.C. § 119(e) based on U.S. Provisional Application No. 60/172,413, filed on December 17, 1999, and U.S. Provisional Application No. 60/126,511, filed on March 26, 1999. This application is also a continuation-in-part of, and claims benefit under 35 U.S.C. § 120 of copending PCT International Application Serial No. US00/07525, filed on March 22, 2000, which claims benefit under 35 U.S.C. § 119(e) based on U.S. Provisional Application No. 60/171,549, filed on December 22, 1999, and U.S. Provisional Application No. 60/126,595, filed on March 26, 1999. This application is also a continuation-in-part of, and claims benefit under 35 U.S.C. § 120 of copending PCT International Application Serial No. US00/07534, filed on March 22, 2000, which claims benefit under 35 U.S.C. § 119(e) based on U.S. Provisional Application No.

60/171,504, filed on December 22, 1999, and U.S. Provisional Application No. 60/126,598, filed on March 26, 1999. This application is also a continuation-in-part of, and claims benefit under 35 U.S.C. § 120 of copending PCT International Application Serial No. US00/07483, filed on March 22, 2000, which claims benefit under 35 U.S.C. § 119(e) based on U.S. Provisional Application No. 60/171,552, filed on December 22, 1999, and U.S. Provisional Application No. 60/126,596, filed on March 26, 1999. This application is also a continuation-in-part of, and claims benefit under 35 U.S.C. § 120 of copending PCT International Application Serial No. US00/07526, filed on March 22, 2000, which claims benefit under 35 U.S.C. § 119(e) based on U.S. Provisional Application No. 60/171,550, filed on December 22, 1999, and U.S. Provisional Application No. 60/126,600, filed on March 26, 1999. This application is also a continuation-in-part of, and claims benefit under 35 U.S.C. § 120 of copending PCT International Application Serial No. US00/07527, filed on March 22, 2000, which claims benefit under 35 U.S.C. § 119(e) based on U.S. Provisional Application No. 60/171,551, filed on December 22, 1999, and U.S. Provisional Application No. 60/126,501, filed on March 26, 1999. This application is also a continuation-in-part of, and claims benefit under 35 U.S.C. § 120 of copending PCT International Application Serial No. US00/07661, filed on March 23, 2000, which claims benefit under 35 U.S.C. § 119(e) based on U.S. Provisional Application No. 60/174,847, filed on January 7, 2000, and U.S. Provisional Application No. 60/126,504, filed on March 26, 1999. This application is also a continuation-in-part of, and claims benefit under 35 U.S.C. § 120 of copending PCT International Application Serial No. US00/07579, filed on March 23, 2000, which claims benefit under 35 U.S.C. § 119(e) based on U.S. Provisional Application No. 60/174,853, filed on January 7, 2000, and U.S. Provisional Application No. 60/126,509, filed on March 26, 1999. This application is also a continuation-in-part of, and claims benefit under 35 U.S.C. § 120 of copending PCT International Application Serial No. US00/07723, filed on March 23, 2000, which claims benefit under 35 U.S.C. § 119(e) based on U.S. Provisional Application No. 60/242,710, filed on October 25, 2000, and U.S. Provisional Application No. 60/174,852, filed on January 7, 2000, and U.S. Provisional Application No. 60/126,506, filed on March 26, 1999. This application is also a continuation-in-part of, and claims benefit under 35 U.S.C. § 120 of copending PCT International Application Serial No. US00/07724, filed on March 23, 2000, which claims benefit under 35 U.S.C. § 119(e) based on U.S. Provisional Application No. 60/174,850, filed on January 7, 2000, and U.S. Provisional Application No. 60/126,510, filed on

March 26, 1999. This application is also a continuation-in-part of, and claims benefit under 35 U.S.C. § 120 of copending PCT International Application Serial No. US00/14929, filed on June 1, 2000, which claims benefit under 35 U.S.C. § 119(e) based on U.S. Provisional Application No. 60/174,851, filed on January 7, 2000, and U.S. Provisional Application No. 60/138,573, filed on June 11, 1999. This application is also a continuation-in-part of, and claims benefit under 35 U.S.C. § 120 of copending PCT International Application Serial No. US00/07722, filed on March 23, 2000, which claims benefit under 35 U.S.C. § 119(e) based on U.S. Provisional Application No. 60/174,871, filed on January 7, 2000, and U.S. Provisional Application No. 60/126,508, filed on March 26, 1999. This application is also a continuation-in-part of, and claims benefit under 35 U.S.C. § 120 of copending PCT International Application Serial No. US00/07578, filed on March 23, 2000, which claims benefit under 35 U.S.C. § 119(e) based on U.S. Provisional Application No. 60/174,872, filed on January 7, 2000, and U.S. Provisional Application No. 60/126,507, filed on March 26, 1999. This application is also a continuation-in-part of, and claims benefit under 35 U.S.C. § 120 of copending PCT International Application Serial No. US00/07726, filed on March 23, 2000, which claims benefit under 35 U.S.C. § 119(e) based on U.S. Provisional Application No. 60/174,877, filed on January 7, 2000, and U.S. Provisional Application No. 60/126,597, filed on March 26, 1999. This application is also a continuation-in-part of, and claims benefit under 35 U.S.C. § 120 of copending PCT International Application Serial No. US00/07677, filed on March 23, 2000, which claims benefit under 35 U.S.C. § 119(e) based on U.S. Provisional Application No. 60/176,064, filed on January 14, 2000, and U.S. Provisional Application No. 60/154,373, filed on September 17, 1999, and U.S. Provisional Application No. 60/126,601, filed on March 26, 1999. This application is also a continuation-in-part of, and claims benefit under 35 U.S.C. § 120 of copending PCT International Application Serial No. US00/07725, filed on March 23, 2000, which claims benefit under 35 U.S.C. § 119(e) based on U.S. Provisional Application No. 60/176,063, filed on January 14, 2000, and U.S. Provisional Application No. 60/126,602, filed on March 26, 1999. This application is also a continuation-in-part of, and claims benefit under 35 U.S.C. § 120 of copending PCT International Application Serial No. US00/09070, filed on April 6, 2000, which claims benefit under 35 U.S.C. § 119(e) based on U.S. Provisional Application No. 60/176,052, filed on January 14, 2000, and U.S. Provisional Application No. 60/128,695, filed on April 9, 1999. This application is also a continuation-in-part of, and claims benefit under 35 U.S.C. § 120 of copending PCT

International Application Serial No. US00/08982, filed on April 6, 2000, which claims benefit under 35 U.S.C. § 119(e) based on U.S. Provisional Application No. 60/176,069, filed on January 14, 2000, and U.S. Provisional Application No. 60/128,696, filed on April 9, 1999. This application is also a continuation-in-part of, and claims benefit under 35 U.S.C. § 120 of copending PCT International Application Serial No. US00/08983, filed on April 6, 2000, which claims benefit under 35 U.S.C. § 119(e) based on U.S. Provisional Application No. 60/176,068, filed on January 14, 2000, and U.S. Provisional Application No. 60/128,703, filed on April 9, 1999. This application is also a continuation-in-part of, and claims benefit under 35 U.S.C. § 120 of copending PCT International Application Serial No. US00/09067, filed on April 6, 2000, which claims benefit under 35 U.S.C. § 119(e) based on U.S. Provisional Application No. 60/176,929, filed on January 20, 2000, and U.S. Provisional Application No. 60/128,697, filed on April 9, 1999. This application is also a continuation-in-part of, and claims benefit under 35 U.S.C. § 120 of copending PCT International Application Serial No. US00/09066, filed on April 6, 2000, which claims benefit under 35 U.S.C. § 119(e) based on U.S. Provisional Application No. 60/176,926, and U.S. Provisional Application No. 60/128,698, filed on April 9, 1999. This application is also a continuation-in-part of, and claims benefit under 35 U.S.C. § 120 of copending PCT International Application Serial No. US00/09068, filed on April 6, 2000, which claims benefit under 35 U.S.C. § 119(e) based on U.S. Provisional Application No. 60/177,050, filed on January 20, 2000, and U.S. Provisional Application No. 60/128,699, filed on April 9, 1999. This application is also a continuation-in-part of, and claims benefit under 35 U.S.C. § 120 of copending PCT International Application Serial No. US00/08981, filed on April 6, 2000, which claims benefit under 35 U.S.C. § 119(e) based on U.S. Provisional Application No. 60/177,166, filed on January 20, 2000, and U.S. Provisional Application No. 60/128,701, filed on April 9, 1999. This application is also a continuation-in-part of, and claims benefit under 35 U.S.C. § 120 of copending PCT International Application Serial No. US00/08980, filed on April 6, 2000, which claims benefit under 35 U.S.C. § 119(e) based on U.S. Provisional Application No. 60/176,930, filed on January 20, 2000, and U.S. Provisional Application No. 60/128,700, filed on April 9, 1999. This application is also a continuation-in-part of, and claims benefit under 35 U.S.C. § 120 of copending PCT International Application Serial No. US00/09071, filed on April 6, 2000, which claims benefit under 35 U.S.C. § 119(e) based on U.S. Provisional Application No. 60/176,931, filed on January 20, 2000, and U.S. Provisional Application No. 60/128,694, filed on

April 9, 1999. This application is also a continuation-in-part of, and claims benefit under 35 U.S.C. § 120 of copending PCT International Application Serial No. US00/09069, filed on April 6, 2000, which claims benefit under 35 U.S.C. § 119(e) based on U.S. Provisional Application No. 60/177,049, filed on January 20, 2000, and U.S. Provisional Application No. 60/128,702, filed on April 9, 1999. This application is also a continuation-in-part of, and claims benefit under 35 U.S.C. § 120 of copending PCT International Application Serial No. US00/15136, filed on June 1, 2000, which claims benefit under 35 U.S.C. § 119(e) based on U.S. Provisional Application No. 60/138,629, filed on June 11, 1999. This application is also a continuation-in-part of, and claims benefit under 35 U.S.C. § 120 of copending PCT International Application Serial No. US00/14926, filed on June 1, 2000, which claims benefit under 35 U.S.C. § 119(e) based on U.S. Provisional Application No. 60/138,628, filed on June 11, 1999. This application is also a continuation-in-part of, and claims benefit under 35 U.S.C. § 120 of copending PCT International Application Serial No. US00/14963, filed on June 1, 2000, which claims benefit under 35 U.S.C. § 119(e) based on U.S. Provisional Application No. 60/138,631, filed on June 11, 1999. This application is also a continuation-in-part of, and claims benefit under 35 U.S.C. § 120 of copending PCT International Application Serial No. US00/15135, filed on June 1, 2000, which claims benefit under 35 U.S.C. § 119(e) based on U.S. Provisional Application No. 60/138,632, filed on June 11, 1999. This application is also a continuation-in-part of, and claims benefit under 35 U.S.C. § 120 of copending PCT International Application Serial No. US00/14934, filed on June 1, 2000, which claims benefit under 35 U.S.C. § 119(e) based on U.S. Provisional Application No. 60/138,599, filed on June 11, 1999. This application is also a continuation-in-part of, and claims benefit under 35 U.S.C. § 120 of copending PCT International Application Serial No. US00/14933, filed on June 1, 2000, which claims benefit under 35 U.S.C. § 119(e) based on U.S. Provisional Application No. 60/138,572, filed on June 11, 1999. This application is also a continuation-in-part of, and claims benefit under 35 U.S.C. § 120 of copending PCT International Application Serial No. US00/15137, filed on June 1, 2000, which claims benefit under 35 U.S.C. § 119(e) based on U.S. Provisional Application No. 60/138,625, filed on June 11, 1999. This application is also a continuation-in-part of, and claims benefit under 35 U.S.C. § 120 of copending PCT International Application Serial No. US00/14928, filed on June 1, 2000, which claims benefit under 35 U.S.C. § 119(e) based on U.S. Provisional Application No. 60/138,633, filed on June 11, 1999. This application is also a continuation-in-part of, and claims benefit under 35 U.S.C. § 120 of

copending PCT International Application Serial No. US00/14973, filed on June 1, 2000, which claims benefit under 35 U.S.C. § 119(e) based on U.S. Provisional Application No. 60/,138,630, filed on June 11, 1999. This application is also a continuation-in-part of, and claims benefit under 35 U.S.C. § 120 of copending PCT International Application Serial No. US00/14964, filed on June 1, 2000, which claims benefit under 35 U.S.C. § 119(e) based on U.S. Provisional Application No. 60/138,627, filed on June 11, 1999. This application is also a continuation-in-part of, and claims benefit under 35 U.S.C. § 120 of copending PCT International Application Serial No. US00/26376, filed on September 26, 2000, which claims benefit under 35 U.S.C. § 119(e) based on U.S. Provisional Application No. 60/155,808, filed on September 27, 1999. This application is also a continuation-in-part of, and claims benefit under 35 U.S.C. § 120 of copending PCT International Application Serial No. US00/26371, filed on September 26, 2000, which claims benefit under 35 U.S.C. § 119(e) based on U.S. Provisional Application No. 60/155,804, filed on September 27, 1999. This application is also a continuation-in-part of, and claims benefit under 35 U.S.C. § 120 of copending PCT International Application Serial No. US00/26324, filed on September 26, 2000, which claims benefit under 35 U.S.C. § 119(e) based on U.S. Provisional Application No. 60/155,807, filed on September 27, 1999. This application is also a continuation-in-part of, and claims benefit under 35 U.S.C. § 120 of copending PCT International Application Serial No. US00/26323, filed on September 26, 2000, which claims benefit under 35 U.S.C. § 119(e) based on U.S. Provisional Application No. 60/155,805, filed on September 27, 1999. This application is also a continuation-in-part of, and claims benefit under 35 U.S.C. § 120 of copending PCT International Application Serial No. US00/26337, filed on September 26, 2000, which claims benefit under 35 U.S.C. § 119(e) based on U.S. Provisional Application No. 60/155,806, filed on September 27, 1999. This application is also a continuation-in-part of, and claims benefit under 35 U.S.C. § 120 of copending PCT International Application Serial No. US01/13318, filed on April 27, 2001, which claims benefit under 35 U.S.C. § 119(e) based on U.S. Provisional Application No. 60/212,142, filed on June 16, 2000, and U.S. Provisional Application No. 60/201,194, filed on May 2, 2000. Each of the above referenced PCT applications were published in the English language. Each of the above referenced priority applications are hereby incorporated by reference in their entireties.

Field of the Invention

[2] The present invention relates to novel proteins. More specifically, isolated nucleic acid molecules are provided encoding novel polypeptides. Novel polypeptides and antibodies that bind to these polypeptides are provided. Also provided are vectors, host cells, and recombinant and synthetic methods for producing human polynucleotides and/or polypeptides, and antibodies. The invention further relates to diagnostic and therapeutic methods useful for diagnosing, treating, preventing and/or prognosing disorders related to these novel polypeptides. The invention further relates to screening methods for identifying agonists and antagonists of polynucleotides and polypeptides of the invention. The present invention further relates to methods and/or compositions for inhibiting or enhancing the production and function of the polypeptides of the present invention.

Background of the Invention

[3] Unlike bacterium, which exist as a single compartment surrounded by a membrane, human cells and other eukaryotes are subdivided by membranes into many functionally distinct compartments. Each membrane-bounded compartment, or organelle, contains different proteins essential for the function of the organelle. The cell uses "sorting signals," which are amino acid motifs located within the protein, to target proteins to particular cellular organelles.

[4] One type of sorting signal, called a signal sequence, a signal peptide, or a leader sequence, directs a class of proteins to an organelle called the endoplasmic reticulum (ER). The ER separates the membrane-bounded proteins from all other types of proteins. Once localized to the ER, both groups of proteins can be further directed to another organelle called the Golgi apparatus. Here, the Golgi distributes the proteins to vesicles, including secretory vesicles, the cell membrane, lysosomes, and the other organelles.

[5] Proteins targeted to the ER by a signal sequence can be released into the extracellular space as a secreted protein. For example, vesicles containing secreted proteins can fuse with the cell membrane and release their contents into the extracellular space - a process called exocytosis. Exocytosis can occur constitutively or after receipt of a triggering signal. In the latter case, the proteins are stored in secretory vesicles (or

secretory granules) until exocytosis is triggered. Similarly, proteins residing on the cell membrane can also be secreted into the extracellular space by proteolytic cleavage of a "linker" holding the protein to the membrane.

[6] Thus there exists a clear need for identifying and using novel secreted polynucleotides and polypeptides. Identification and sequencing of human genes is a major goal of modern scientific research. For example, by identifying genes and determining their sequences, scientists have been able to make large quantities of valuable human "gene products." These include human insulin, interferon, Factor VIII, tumor necrosis factor, human growth hormone, tissue plasminogen activator, and numerous other compounds. Additionally, knowledge of gene sequences can provide the key to treatment or cure of genetic diseases (such as muscular dystrophy and cystic fibrosis).

Summary of the Invention

[7] The present invention relates to novel secreted proteins. More specifically, isolated nucleic acid molecules are provided encoding novel secreted polypeptides. Novel polypeptides and antibodies that bind to these polypeptides are provided. Also provided are vectors, host cells, and recombinant and synthetic methods for producing human polynucleotides and/or polypeptides, and antibodies. The invention further relates to diagnostic and therapeutic methods useful for diagnosing, treating, preventing and/or prognosing disorders related to these novel polypeptides. The invention further relates to screening methods for identifying agonists and antagonists of polynucleotides and polypeptides of the invention. The present invention further relates to methods and/or compositions for inhibiting or enhancing the production and function of the polypeptides of the present invention.

Detailed Description

Polynucleotides and Polypeptides

Description of Table 1A

[8] Table 1A summarizes information concerning certain polypnucleotides and polypeptides of the invention. The first column provides the gene number in the

application for each clone identifier. The second column provides a unique clone identifier, "Clone ID NO:Z", for a cDNA clone related to each contig sequence disclosed in Table 1A. Third column, the cDNA Clones identified in the second column were deposited as indicated in the third column (i.e. by ATCC Deposit Number and deposit date). Some of the deposits contain multiple different clones corresponding to the same gene. In the fourth column, "Vector" refers to the type of vector contained in the corresponding cDNA Clone identified in the second column. In the fifth column, the nucleotide sequence identified as "NT SEQ ID NO:X" was assembled from partially homologous ("overlapping") sequences obtained from the corresponding cDNA clone identified in the second column and, in some cases, from additional related cDNA clones. The overlapping sequences were assembled into a single contiguous sequence of high redundancy (usually three to five overlapping sequences at each nucleotide position), resulting in a final sequence identified as SEQ ID NO:X. In the sixth column, "Total NT Seq." refers to the total number of nucleotides in the contig sequence identified as SEQ ID NO:X." The deposited clone may contain all or most of these sequences, reflected by the nucleotide position indicated as "5' NT of Clone Seq." (seventh column) and the "3' NT of Clone Seq." (eighth column) of SEQ ID NO:X. In the ninth column, the nucleotide position of SEQ ID NO:X of the putative start codon (methionine) is identified as "5' NT of Start Codon." Similarly , in column ten, the nucleotide position of SEQ ID NO:X of the predicted signal sequence is identified as "5' NT of First AA of Signal Pep." In the eleventh column, the translated amino acid sequence, beginning with the methionine, is identified as "AA SEQ ID NO:Y," although other reading frames can also be routinely translated using known molecular biology techniques. The polypeptides produced by these alternative open reading frames are specifically contemplated by the present invention.

[9] In the twelfth and thirteenth columns of Table 1A, the first and last amino acid position of SEQ ID NO:Y of the predicted signal peptide is identified as "First AA of Sig Pep" and "Last AA of Sig Pep." In the fourteenth column, the predicted first amino acid position of SEQ ID NO:Y of the secreted portion is identified as "Predicted First AA of Secreted Portion". The amino acid position of SEQ ID NO:Y of the last amino acid encoded by the open reading frame is identified in the fifteenth column as "Last AA of ORF".

[10] SEQ ID NO:X (where X may be any of the polynucleotide sequences disclosed in the sequence listing) and the translated SEQ ID NO:Y (where Y may be any of the polypeptide sequences disclosed in the sequence listing) are sufficiently accurate and otherwise suitable for a variety of uses well known in the art and described further below. For instance, SEQ ID NO:X is useful for designing nucleic acid hybridization probes that will detect nucleic acid sequences contained in SEQ ID NO:X or the cDNA contained in the deposited clone. These probes will also hybridize to nucleic acid molecules in biological samples, thereby enabling a variety of forensic and diagnostic methods of the invention. Similarly, polypeptides identified from SEQ ID NO:Y may be used, for example, to generate antibodies which bind specifically to proteins containing the polypeptides and the secreted proteins encoded by the cDNA clones identified in Table 1A and/or elsewhere herein

[11] Nevertheless, DNA sequences generated by sequencing reactions can contain sequencing errors. The errors exist as misidentified nucleotides, or as insertions or deletions of nucleotides in the generated DNA sequence. The erroneously inserted or deleted nucleotides cause frame shifts in the reading frames of the predicted amino acid sequence. In these cases, the predicted amino acid sequence diverges from the actual amino acid sequence, even though the generated DNA sequence may be greater than 99.9% identical to the actual DNA sequence (for example, one base insertion or deletion in an open reading frame of over 1000 bases).

[12] Accordingly, for those applications requiring precision in the nucleotide sequence or the amino acid sequence, the present invention provides not only the generated nucleotide sequence identified as SEQ ID NO:X, and the predicted translated amino acid sequence identified as SEQ ID NO:Y, but also a sample of plasmid DNA containing a human cDNA of the invention deposited with the ATCC, as set forth in Table 1A. The nucleotide sequence of each deposited plasmid can readily be determined by sequencing the deposited plasmid in accordance with known methods

[13] The predicted amino acid sequence can then be verified from such deposits. Moreover, the amino acid sequence of the protein encoded by a particular plasmid can also be directly determined by peptide sequencing or by expressing the protein in a suitable host cell containing the deposited human cDNA, collecting the protein, and determining its sequence.

[14] Also provided in Table 1A is the name of the vector which contains the cDNA plasmid. Each vector is routinely used in the art. The following additional information is provided for convenience.

[15] Vectors Lambda Zap (U.S. Patent Nos. 5,128,256 and 5,286,636), Uni-Zap XR (U.S. Patent Nos. 5,128, 256 and 5,286,636), Zap Express (U.S. Patent Nos. 5,128,256 and 5,286,636), pBluescript (pBS) (Short, J. M. et al., *Nucleic Acids Res. 16:*7583-7600 (1988); Alting-Mees, M. A. and Short, J. M., *Nucleic Acids Res. 17:*9494 (1989)) and pBK (Alting-Mees, M. A. et al., *Strategies 5:*58-61 (1992)) are commercially available from Stratagene Cloning Systems, Inc., 11011 N. Torrey Pines Road, La Jolla, CA, 92037. pBS contains an ampicillin resistance gene and pBK contains a neomycin resistance gene. Phagemid pBS may be excised from the Lambda Zap and Uni-Zap XR vectors, and phagemid pBK may be excised from the Zap Express vector. Both phagemids may be transformed into *E. coli* strain XL-1 Blue, also available from Stratagene

[16] Vectors pSport1, pCMVSport 1.0, pCMVSport 2.0 and pCMVSport 3.0, were obtained from Life Technologies, Inc., P. O. Box 6009, Gaithersburg, MD 20897. All Sport vectors contain an ampicillin resistance gene and may be transformed into *E. coli* strain DH10B, also available from Life Technologies. See, for instance, Gruber, C. E., et al., *Focus 15:*59 (1993). Vector lafmid BA (Bento Soares, Columbia University, New York, NY) contains an ampicillin resistance gene and can be transformed into *E. coli* strain XL-1 Blue. Vector pCR®2.1, which is available from Invitrogen, 1600 Faraday Avenue, Carlsbad, CA 92008, contains an ampicillin resistance gene and may be transformed into *E. coli* strain DH10B, available from Life Technologies. See, for instance, Clark, J. M., *Nuc. Acids Res. 16:*9677-9686 (1988) and Mead, D. *et al., Bio/Technology 9:* (1991).

[17] The present invention also relates to the genes corresponding to SEQ ID NO:X, SEQ ID NO:Y, and/or a deposited cDNA (cDNA Clone ID). The corresponding gene can be isolated in accordance with known methods using the sequence information disclosed herein. Such methods include, but are not limited to, preparing probes or primers from the disclosed sequence and identifying or amplifying the corresponding gene from appropriate sources of genomic material.

[18] Also provided in the present invention are allelic variants, orthologs, and/or species homologs. Procedures known in the art can be used to obtain full-length genes, allelic variants, splice variants, full-length coding portions, orthologs, and/or species homologs of genes corresponding to SEQ ID NO:X and SEQ ID NO:Y using information

from the sequences disclosed herein or the clones deposited with the ATCC. For example, allelic variants and/or species homologs may be isolated and identified by making suitable probes or primers from the sequences provided herein and screening a suitable nucleic acid source for allelic variants and/or the desired homologue.

[19] The present invention provides a polynucleotide comprising, or alternatively consisting of, the nucleic acid sequence of SEQ ID NO:X and/or a cDNA contained in ATCC Deposit No.Z. The present invention also provides a polypeptide comprising, or alternatively, consisting of, the polypeptide sequence of SEQ ID NO:Y, a polypeptide encoded by SEQ ID NO:X, and/or a polypeptide encoded by a cDNA contained in ATCC deposit No.Z. Polynucleotides encoding a polypeptide comprising, or alternatively consisting of the polypeptide sequence of SEQ ID NO:Y, a polypeptide encoded by SEQ ID NO:X and/or a polypeptide encoded by the cDNA contained in ATCC Deposit No.Z, are also encompassed by the invention. The present invention further encompasses a polynucleotide comprising, or alternatively consisting of the complement of the nucleic acid sequence of SEQ ID NO:X, and/or the complement of the coding strand of the cDNA contained in ATCC Deposit No.Z.

Description of Table 1B

[20] Table 1B summarizes some of the polynucleotides encompassed by the invention (including cDNA clones related to the sequences (Clone ID NO:Z), contig sequences (contig identifier (Contig ID:) and contig nucleotide sequence identifier (SEQ ID NO:X)) and further summarizes certain characteristics of these polynucleotides and the polypeptides encoded thereby. The first column provides the gene number in the application for each clone identifier. The second column provides a unique clone identifier, "Clone ID NO:Z", for a cDNA clone related to each contig sequence disclosed in Table 1A and/or 1B. The third column provides a unique contig identifier, "Contig ID:" for each of the contig sequences disclosed in Table 1B. The fourth column provides the sequence identifier, "SEQ ID NO:X", for each of the contig sequences disclosed in Table 1A and/or 1B. The fifth column, "ORF (From-To)", provides the location (i.e., nucleotide position numbers) within the polynucleotide sequence of SEQ ID NO:X that delineate the preferred open reading frame (ORF) that encodes the amino acid sequence shown in the sequence listing and referenced in Table 1B as SEQ ID NO:Y (column 6). Column 7 lists residues comprising predicted epitopes contained in the polypeptides encoded by each of the preferred ORFs (SEQ ID NO:Y). Identification of potential

immunogenic regions was performed according to the method of Jameson and Wolf (CABIOS, 4; 181-186 (1988)); specifically, the Genetics Computer Group (GCG) implementation of this algorithm, embodied in the program PEPTIDESTRUCTURE (Wisconsin Package v10.0, Genetics Computer Group (GCG), Madison, Wisc.). This method returns a measure of the probability that a given residue is found on the surface of the protein. Regions where the antigenic index score is greater than 0.9 over at least 6 amino acids are indicated in Table 1B as "Predicted Epitopes". In particular embodiments, polypeptides of the invention comprise, or alternatively consist of, one, two, three, four, five or more of the predicted epitopes described in Table 1B. It will be appreciated that depending on the analytical criteria used to predict antigenic determinants, the exact address of the determinant may vary slightly. Column 8, "Tissue Distribution" shows the expression profile of tissue, cells, and/or cell line libraries which express the polynucleotides of the invention. The first number in column 8 (preceding the colon), represents the tissue/cell source identifier code corresponding to the key provided in Table 4. Expression of these polynucleotides was not observed in the other tissues and/or cell libraries tested. For those identifier codes in which the first two letters are not "AR", the second number in column 8 (following the colon), represents the number of times a sequence corresponding to the reference polynucleotide sequence (e.g., SEQ ID NO:X) was identified in the tissue/cell source. Those tissue/cell source identifier codes in which the first two letters are "AR" designate information generated using DNA array technology. Utilizing this technology, cDNAs were amplified by PCR and then transferred, in duplicate, onto the array. Gene expression was assayed through hybridization of first strand cDNA probes to the DNA array. cDNA probes were generated from total RNA extracted from a variety of different tissues and cell lines. Probe synthesis was performed in the presence of ^{33}P dCTP, using oligo(dT) to prime reverse transcription. After hybridization, high stringency washing conditions were employed to remove non-specific hybrids from the array. The remaining signal, emanating from each gene target, was measured using a Phosphorimager. Gene expression was reported as Phosphor Stimulating Luminescence (PSL) which reflects the level of phosphor signal generated from the probe hybridized to each of the gene targets represented on the array. A local background signal subtraction was performed before the total signal generated from each array was used to normalize gene expression between the different hybridizations. The value presented after "[array code]:" represents the mean of the duplicate values, following background subtraction and probe normalization. One of skill

in the art could routinely use this information to identify normal and/or diseased tissue(s) which show a predominant expression pattern of the corresponding polynucleotide of the invention or to identify polynucleotides which show predominant and/or specific tissue and/or cell expression. Column 9 provides the chromosomal location of polynucleotides corresponding to SEQ ID NO:X. Chromosomal location was determined by finding exact matches to EST and cDNA sequences contained in the NCBI (National Center for Biotechnology Information) UniGene database. Given a presumptive chromosomal location, disease locus association was determined by comparison with the Morbid Map, derived from Online Mendelian Inheritance in Man (Online Mendelian Inheritance in Man, OMIM™. McKusick-Nathans Institute for Genetic Medicine, Johns Hopkins University (Baltimore, MD) and National Center for Biotechnology Information, National Library of Medicine (Bethesda, MD) 2000. World Wide Web URL: http://www.ncbi.nlm.nih.gov/omim/). If the putative chromosomal location of the Query overlaps with the chromosomal location of a Morbid Map entry, an OMIM identification number is disclosed in column **10** labeled "OMIM Disease Reference(s)". A key to the OMIM reference identification numbers is provided in Table 5.

Description of Table 1C

[21] Table 1C summarizes additional polynucleotides encompassed by the invention (including cDNA clones related to the sequences (Clone ID NO:Z), contig sequences (contig identifier (Contig ID:) contig nucleotide sequence identifiers (SEQ ID NO:X)), and genomic sequences (SEQ ID NO:B). The first column provides a unique clone identifier, "Clone ID NO:Z", for a cDNA clone related to each contig sequence. The second column provides the sequence identifier, "SEQ ID NO:X", for each contig sequence. The third column provides a unique contig identifier, "Contig ID:" for each contig sequence. The fourth column, provides a BAC identifier "BAC ID NO:A" for the BAC clone referenced in the corresponding row of the table. The fifth column provides the nucleotide sequence identifier, "SEQ ID NO:B" for a fragment of the BAC clone identified in column four of the corresponding row of the table. The sixth column, "Exon From-To", provides the location (i.e., nucleotide position numbers) within the polynucleotide sequence of SEQ ID NO:B which delineate certain polynucleotides of the invention that are also exemplary members of polynucleotide sequences that encode polypeptides of the invention (e.g., polypeptides containing amino acid sequences encoded

by the polynucleotide sequences delineated in column six, and fragments and variants thereof).

Description of Table 1D

[22] Table 1D: In preferred embodiments, the present invention encompasses a method of treating a disease or disorder listed in the "FEATURES OF PROTEIN" sections (below) and also as listed in the "Preferred Indications" column of Table 1D (below); comprising administering to a patient in which such treatment, prevention, or amelioration is desired a protein, nucleic acid, or antibody of the invention (or fragment or variant thereof) represented by Table 1A and Table 1D (in the same row as the disease or disorder to be treated is listed in the "Preferred Indications" column of Table 1D) in an amount effective to treat, prevent, or ameliorate the disease or disorder.

[23] As indicated in Table 1D, the polynucleotides, polypeptides, agonists, or antagonists of the present invention (including antibodies) can be used in assays to test for one or more biological activities. If these polynucleotides and polypeptides do exhibit activity in a particular assay, it is likely that these molecules may be involved in the diseases associated with the biological activity. Thus, the polynucleotides or polypeptides, or agonists or antagonists thereof (including antibodies) could be used to treat the associated disease.

[24] The present invention encompasses methods of preventing, treating, diagnosing, or ameliorating a disease or disorder. In preferred embodiments, the present invention encompasses a method of treating a disease or disorder listed in the "Preferred Indications" column of Table 1D; comprising administering to a patient in which such treatment, prevention, or amelioration is desired a protein, nucleic acid, or antibody of the invention (or fragment or variant thereof) in an amount effective to treat, prevent, diagnose, or ameliorate the disease or disorder. The first and seccond columns of Table 1D show the "Gene No." and "cDNA Clone ID No.", respectively, indicating certain nucleic acids and proteins (or antibodies against the same) of the invention (including polynucleotide, polypeptide, and antibody fragments or variants thereof) that may be used in preventing, treating, diagnosing, or ameliorating the disease(s) or disorder(s) indicated in the corresponding row in Column 3 of Table 1D.

[25] In another embodiment, the present invention also encompasses methods of preventing, treating, diagnosing, or ameliorating a disease or disorder listed in the "Preferred Indications" column of Table 1D; comprising administering to a patient

combinations of the proteins, nucleic acids, or antibodies of the invention (or fragments or variants thereof), sharing similar indications as shown in the corresponding rows in Column 3 of Table 1D.

[26] The "Preferred Indication" column describes diseases, disorders, and/or conditions that may be treated, prevented, diagnosed, or ameliorated by a protein, nucleic acid, or antibody of the invention (or fragment or variant thereof).

[27] The recitation of "Cancer" in the "Preferred Indication" column indicates that the corresponding nucleic acid and protein, or antibody against the same, of the invention (or fragment or variant thereof) may be used for example, to diagnose, treat, prevent, and/or ameliorate diseases and/or disorders relating to neoplastic diseases (e.g., leukemias, cancers, and/or as described below under "Hyperproliferative Disorders").

[28] In specific embodiments, a protein, nucleic acid, or antibody of the invention (or fragment or variant thereof) having a "Cancer" recitation in the "Preferred Indication" column of Table 1D may be used for example, to diagnose, treat, prevent, and/or ameliorate a neoplasm located in a tissue selected from the group consisting of: colon, abdomen, bone, breast, digestive system, liver, pancreas, prostate, peritoneum, lung, blood (e.g., leukemia), endocrine glands (adrenal, parathyroid, pituitary, testicles, ovary, thymus, thyroid), uterus, eye, head and neck, nervous (central and peripheral), lymphatic system, pelvic, skin, soft tissue, spleen, thoracic, and urogenital.

[29] In specific embodiments, a protein, nucleic acid, or antibody of the invention (or fragment or variant thereof) having a "Cancer" recitation in the "Preferred Indication" column of Table 1D, may be used for example, to diagnose, treat, prevent, and/or ameliorate a pre-neoplastic condition, selected from the group consisting of: hyperplasia (e.g., endometrial hyperplasia and/or as described in the section entitled "Hyperproliferative Disorders"), metaplasia (e.g., connective tissue metaplasia, atypical metaplasia, and/or as described in the section entitled "Hyperproliferative Disorders"), and/or dysplasia (e.g., cervical dysplasia, and bronchopulmonary dysplasia).

[30] In another specific embodiment, a protein, nucleic acid, or antibody of the invention (or fragment or variant thereof) having a "Cancer" recitation in the "Preferred Indication" column of Table 1D, may be used for example, to diagnose, treat, prevent, and/or ameliorate a benign dysproliferative disorder selected from the group consisting of: benign tumors, fibrocystic conditions, tissue hypertrophy, and/or as described in the section entitled "Hyperproliferative Disorders".

[31] The recitation of "Immune/Hematopoietic" in the "Preferred Indication" column indicates that the corresponding nucleic acid and protein, or antibody against the same, of the invention (or fragment or variant thereof), may be used for example, to diagnose, treat, prevent, and/or ameliorate diseases and/or disorders relating to neoplastic diseases (e.g., as described below under "Hyperproliferative Disorders"), blood disorders (e.g., as described below under "Immune Activity" "Cardiovascular Disorders" and/or "Blood-Related Disorders"), and infections (e.g., as described below under "Infectious Disease").

[32] In specific embodiments, a protein, nucleic acid, or antibody of the invention (or fragment or variant thereof) having the "Immune/Hematopoietic" recitation in the "Preferred Indication" column of Table 1D, may be used for example, to diagnose, treat, prevent, and/or ameliorate a disease or disorder selected from the group consisting of: anemia, pancytopenia, leukopenia, thrombocytopenia, leukemias, Hodgkin's disease, non-Hodgkin's lymphoma, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, asthma, AIDS, autoimmune disease, rheumatoid arthritis, granulomatous disease, immune deficiency, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, immune reactions to transplanted organs and tissues, systemic lupus erythematosis, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, and allergies.

[33] The recitation of "Reproductive" in the "Preferred Indication" column indicates that the corresponding nucleic acid and protein, or antibody against the same, of the invention (or fragment or variant thereof), may be used for example, to diagnose, treat, prevent, and/or ameliorate diseases and/or disorders relating to neoplastic diseases (e.g., as described below under "Hyperproliferative Disorders"), and disorders of the reproductive system (e.g., as described below under "Reproductive System Disorders").

[34] In specific embodiments, a protein, nucleic acid, or antibody of the invention (or fragment or variant thereof) having a "Reproductive" recitation in the "Preferred Indication" column of Table 1D, may be used for example, to diagnose, treat, prevent, and/or ameliorate a disease or disorder selected from the group consisting of: cryptorchism, prostatitis, inguinal hernia, varicocele, leydig cell tumors, verrucous carcinoma, prostatitis, malacoplakia, Peyronie's disease, penile carcinoma, squamous cell hyperplasia, dysmenorrhea, ovarian adenocarcinoma, Turner's syndrome, mucopurulent cervicitis, Sertoli-leydig tumors, ovarian cancer, uterine cancer, pelvic inflammatory disease, testicular cancer, prostate cancer, Klinefelter's syndrome, Young's syndrome,

premature ejaculation, diabetes mellitus, cystic fibrosis, Kartagener's syndrome, testicular atrophy, testicular feminization, anorchia, ectopic testis, epididymitis, orchitis, gonorrhea, syphilis, testicular torsion, vasitis nodosa, germ cell tumors, stromal tumors, dysmenorrhea, retroverted uterus, endometriosis, fibroids, adenomyosis, anovulatory bleeding, amenorrhea, Cushing's syndrome, hydatidiform moles, Asherman's syndrome, premature menopause, precocious puberty, uterine polyps, dysfunctional uterine bleeding, cervicitis, chronic cervicitis, mucopurulent cervicitis, cervical dysplasia, cervical polyps, Nabothian cysts, cervical erosion, cervical incompetence, cervical neoplasms, pseudohermaphroditism, and premenstrual syndrome.

[35] The recitation of "Musculoskeletal" in the "Preferred Indication" column indicates that the corresponding nucleic acid and protein, or antibody against the same, of the invention (or fragment or variant thereof), may be used for example, to diagnose, treat, prevent, and/or ameliorate diseases and/or disorders relating to neoplastic diseases (e.g., as described below under "Hyperproliferative Disorders"), and disorders of the immune system (e.g., as described below under "Immune Activity").

[36] In specific embodiments, a protein, nucleic acid, or antibody of the invention (or fragment or variant thereof) having a "Musculoskeletal" recitation in the "Preferred Indication" column of Table 1D, may be used for example, to diagnose, treat, prevent, and/or ameliorate a disease or disorder selected from the group consisting of: bone cancers (e.g., osteochondromas, benign chondromas, chondroblastoma, chondromyxoid fibromas, osteoid osteomas, giant cell tumors, multiple myeloma, osteosarcomas), Paget's Disease, rheumatoid arthritis, systemic lupus erythematosus, osteomyelitis, Lyme Disease, gout, bursitis, tendonitis, osteoporosis, osteoarthritis, muscular dystrophy, mitochondrial myopathy, cachexia, and multiple sclerosis.

[37] The recitation of "Cardiovascular" in the "Preferred Indication" column indicates that the corresponding nucleic acid and protein, or antibody against the same, of the invention (or fragment or variant thereof), may be used for example, to diagnose, treat, prevent, and/or ameliorate diseases and/or disorders relating to neoplastic diseases (e.g., as described below under "Hyperproliferative Disorders"), and disorders of the cardiovascular system (e.g., as described below under "Cardiovascular Disorders").

[38] In specific embodiments, a protein, nucleic acid, or antibody of the invention (or fragment or variant thereof) having a "Cardiovascular" recitation in the "Preferred Indication" column of Table 1D, may be used for example, to diagnose, treat, prevent, and/or ameliorate a disease or disorder selected from the group consisting of: myxomas,

fibromas, rhabdomyomas, cardiovascular abnormalities (e.g., congenital heart defects, cerebral arteriovenous malformations, septal defects), heart disease (e.g., heart failure, congestive heart disease, arrhythmia, tachycardia, fibrillation, pericardial Disease, endocarditis), cardiac arrest, heart valve disease (e.g., stenosis, regurgitation, prolapse), vascular disease (e.g., hypertension, coronary artery disease, angina, aneurysm, arteriosclerosis, peripheral vascular disease), hyponatremia, hypernatremia, hypokalemia, and hyperkalemia.

[39] The recitation of "Mixed Fetal" in the "Preferred Indication" column indicates that the corresponding nucleic acid and protein, or antibody against the same, of the invention (or fragment or variant thereof), may be used for example, to diagnose, treat, prevent, and/or ameliorate diseases and/or disorders relating to neoplastic diseases (e.g., as described below under "Hyperproliferative Disorders").

[40] In specific embodiments, a protein, nucleic acid, or antibody of the invention (or fragment or variant thereof) having a "Mixed Fetal" recitation in the "Preferred Indication" column of Table 1D, may be used for example, to diagnose, treat, prevent, and/or ameliorate a disease or disorder selected from the group consisting of: spina bifida, hydranencephaly, neurofibromatosis, fetal alcohol syndrome, diabetes mellitus, PKU, Down's syndrome, Patau syndrome, Edwards syndrome, Turner syndrome, Apert syndrome, Carpenter syndrome, Conradi syndrome, Crouzon syndrome, cutis laxa, Cornelia de Lange syndrome, Ellis-van Creveld syndrome, Holt-Oram syndrome, Kartagener syndrome, Meckel-Gruber syndrome, Noonan syndrome, Pallister-Hall syndrome, Rubinstein-Taybi syndrome, Scimitar syndrome, Smith-Lemli-Opitz syndrome, thromocytopenia-absent radius (TAR) syndrome, Treacher Collins syndrome, Williams syndrome, Hirschsprung's disease, Meckel's diverticulum, polycystic kidney disease, Turner's syndrome, and gonadal dysgenesis, Klippel-Feil syndrome, Ostogenesis imperfecta, muscular dystrophy, Tay-Sachs disease, Wilm's tumor, neuroblastoma, and retinoblastoma.

[41] The recitation of "Excretory" in the "Preferred Indication" column indicates that the corresponding nucleic acid and protein, or antibody against the same, of the invention (or fragment or variant thereof), may be used for example, to diagnose, treat, prevent, and/or ameliorate diseases and/or disorders relating to neoplastic diseases (e.g., as described below under "Hyperproliferative Disorders") and renal disorders (e.g., as described below under "Renal Disorders").

[42] In specific embodiments, a protein, nucleic acid, or antibody of the invention (or fragment or variant thereof) having a "Excretory" recitation in the "Preferred Indication" column of Table 1D, may be used for example, to diagnose, treat, prevent, and/or ameliorate a disease or disorder selected from the group consisting of: bladder cancer, prostate cancer, benign prostatic hyperplasia, bladder disorders (e.g., urinary incontinence, urinary retention, urinary obstruction, urinary tract Infections, interstitial cystitis, prostatitis, neurogenic bladder, hematuria), renal disorders (e.g., hydronephrosis, proteinuria, renal failure, pyelonephritis, urolithiasis, reflux nephropathy, and unilateral obstructive uropathy).

[43] The recitation of "Neural/Sensory" in the "Preferred Indication" column indicates that the corresponding nucleic acid and protein, or antibody against the same, of the invention (or fragment or variant thereof), may be used for example, to diagnose, treat, prevent, and/or ameliorate diseases and/or disorders relating to neoplastic diseases (e.g., as described below under "Hyperproliferative Disorders") and diseases or disorders of the nervous system (e.g., as described below under "Neural Activity and Neurological Diseases").

[44] In specific embodiments, a protein, nucleic acid, or antibody of the invention (or fragment or variant thereof) having a "Neural/Sensory" recitation in the "Preferred Indication" column of Table 1D, may be used for example, to diagnose, treat, prevent, and/or ameliorate a disease or disorder selected from the group consisting of: brain cancer (e.g., brain stem glioma, brain tumors, central nervous system (Primary) lymphoma, central nervous system lymphoma, cerebellar astrocytoma, and cerebral astrocytoma, neurodegenerative disorders (e.g., Alzheimer's Disease, Creutzfeldt-Jakob Disease, Parkinson's Disease, and Idiopathic Presenile Dementia), encephalomyelitis, cerebral malaria, meningitis, metabolic brain diseases (e.g., phenylketonuria and pyruvate carboxylase deficiency), cerebellar ataxia, ataxia telangiectasia, and AIDS Dementia Complex, schizophrenia, attention deficit disorder, hyperactive attention deficit disorder, autism, and obsessive compulsive disorders.

[45] The recitation of "Respiratory" in the "Preferred Indication" column indicates that the corresponding nucleic acid and protein, or antibody against the same, of the invention (or fragment or variant thereof), may be used for example, to diagnose, treat, prevent, and/or ameliorate diseases and/or disorders relating to neoplastic diseases (e.g., as described below under "Hyperproliferative Disorders") and diseases or disorders of the respiratory system (e.g., as described below under "Respiratory Disorders").

[46] In specific embodiments, a protein, nucleic acid, or antibody of the invention (or fragment or variant thereof) having a "Respiratory" recitation in the "Preferred Indication" column of Table 1D, may be used for example, to diagnose, treat, prevent, and/or ameliorate a disease or disorder selected from the group consisting of: cancers of the respiratory system such as larynx cancer, pharynx cancer, trachea cancer, epiglottis cancer, lung cancer, squamous cell carcinomas, small cell (oat cell) carcinomas, large cell carcinomas, and adenocarcinomas. Allergic reactions, cystic fibrosis, sarcoidosis, histiocytosis X, infiltrative lung diseases (e.g., pulmonary fibrosis and lymphoid interstitial pneumonia), obstructive airway diseases (e.g., asthma, emphysema, chronic or acute bronchitis), occupational lung diseases (e.g., silicosis and asbestosis), pneumonia, and pleurisy.

[47] The recitation of "Endocrine" in the "Preferred Indication" column indicates that the corresponding nucleic acid and protein, or antibody against the same, of the invention (or fragment or variant thereof), may be used for example, to diagnose, treat, prevent, and/or ameliorate diseases and/or disorders relating to neoplastic diseases (e.g., as described below under "Hyperproliferative Disorders") and diseases or disorders of the respiratory system (e.g., as described below under "Respiratory Disorders"), renal disorders (e.g., as described below under "Renal Disorders"), and disorders of the endocrine system (e.g., as described below under "Endocrine Disorders".

[48] In specific embodiments, a protein, nucleic acid, or antibody of the invention (or fragment or variant thereof) having an "Endocrine" recitation in the "Preferred Indication" column of Table 1D, may be used for example, to diagnose, treat, prevent, and/or ameliorate a disease or disorder selected from the group consisting of: cancers of endocrine tissues and organs (e.g., cancers of the hypothalamus, pituitary gland, thyroid gland, parathyroid glands, pancreas, adrenal glands, ovaries, and testes), diabetes (e.g., diabetes insipidus, type I and type II diabetes mellitus), obesity, disorders related to pituitary glands (e.g., hyperpituitarism, hypopituitarism, and pituitary dwarfism), hypothyroidism, hyperthyroidism, goiter, reproductive disorders (e.g. male and female infertility), disorders related to adrenal glands (e.g., Addison's Disease, corticosteroid deficiency, and Cushing's Syndrome), kidney cancer (e.g., hypernephroma, transitional cell cancer, and Wilm's tumor), diabetic nephropathy, interstitial nephritis, polycystic kidney disease, glomerulonephritis (e.g., IgM mesangial proliferative glomerulonephritis and glomerulonephritis caused by autoimmune disorders; such as Goodpasture's syndrome), and nephrocalcinosis.

[49] The recitation of "Digestive" in the "Preferred Indication" column indicates that the corresponding nucleic acid and protein, or antibody against the same, of the invention (or fragment or variant thereof), may be used for example, to diagnose, treat, prevent, and/or ameliorate diseases and/or disorders relating to neoplastic diseases (e.g., as described below under "Hyperproliferative Disorders") and diseases or disorders of the gastrointestinal system (e.g., as described below under "Gastrointestinal Disorders".

[50] In specific embodiments, a protein, nucleic acid, or antibody of the invention (or fragment or variant thereof) having a "Digestive" recitation in the "Preferred Indication" column of Table 1D, may be used for example, to diagnose, treat, prevent, and/or ameliorate a disease or disorder selected from the group consisting of: ulcerative colitis, appendicitis, Crohn's disease, hepatitis, hepatic encephalopathy, portal hypertension, cholelithiasis, cancer of the digestive system (e.g., biliary tract cancer, stomach cancer, colon cancer, gastric cancer, pancreatic cancer, cancer of the bile duct, tumors of the colon (e.g., polyps or cancers), and cirrhosis), pancreatitis, ulcerative disease, pyloric stenosis, gastroenteritis, gastritis, gastric atropy, benign tumors of the duodenum, distension, irritable bowel syndrome, malabsorption, congenital disorders of the small intestine, bacterial and parasitic infection, megacolon, Hirschsprung's disease, aganglionic megacolon, acquired megacolon, colitis, anorectal disorders (e.g., anal fistulas, hemorrhoids), congenital disorders of the liver (e.g., Wilson's disease, hemochromatosis, cystic fibrosis, biliary atresia, and alpha1-antitrypsin deficiency), portal hypertension, cholelithiasis, and jaundice.

[51] The recitation of "Connective/Epithelial" in the "Preferred Indication" column indicates that the corresponding nucleic acid and protein, or antibody against the same, of the invention (or fragment or variant thereof), may be used for example, to diagnose, treat, prevent, and/or ameliorate diseases and/or disorders relating to neoplastic diseases (e.g., as described below under "Hyperproliferative Disorders"), cellular and genetic abnormalities (e.g., as described below under "Diseases at the Cellular Level "), angiogenesis (e.g., as described below under "Anti-Angiogenesis Activity "), and or to promote or inhibit regeneration (e.g., as described below under "Regeneration "), and wound healing (e.g., as described below under "Wound Healing and Epithelial Cell Proliferation").

[52] In specific embodiments, a protein, nucleic acid, or antibody of the invention (or fragment or variant thereof) having a "Connective/Epithelial" recitation in the "Preferred Indication" column of Table 1D, may be used for example, to diagnose, treat, prevent, and/or ameliorate a disease or disorder selected from the group consisting of:

connective tissue metaplasia, mixed connective tissue disease, focal epithelial hyperplasia, epithelial metaplasia, mucoepithelial dysplasia, graft v. host disease, polymyositis, cystic hyperplasia, cerebral dysplasia, tissue hypertrophy, Alzheimer's disease, lymphoproliferative disorder, Waldenstron's macroglobulinemia, Crohn's disease, pernicious anemia, idiopathic Addison's disease, glomerulonephritis, bullous pemphigoid, Sjogren's syndrome, diabetes mellitus, cystic fibrosis, osteoblastoma, osteoclastoma, osteosarcoma, chondrosarcoma, osteoporosis, osteocarthritis, periodontal disease, wound healing, relapsing polychondritis, vasculitis, polyarteritis nodosa, Wegener's granulomatosis, cellulitis, rheumatoid arthritis, psoriatic arthritis, discoid lupus erythematosus, systemic lupus erythematosus, scleroderma, CREST syndrome, Sjogren's syndrome, polymyositis, dermatomyositis, mixed connective tissue disease, relapsing polychondritis, vasculitis, Henoch-Schonlein syndrome, erythema nodosum, polyarteritis nodosa, temporal (giant cell) arteritis, Takayasu's arteritis, Wegener's granulomatosis, Reiter's syndrome, Behcet's syndrome, ankylosing spondylitis, cellulitis, keloids, Ehler Danlos syndrome, Marfan syndrome, pseudoxantoma elasticum, osteogenese imperfecta, chondrodysplasias, epidermolysis bullosa, Alport syndrome, and cutis laxa.

Description of Table 2

[53] Table 2 summarizes homology and features of some of the polypeptides of the invention. The first column provides a unique clone identifier, "Clone ID NO:Z", corresponding to a cDNA clone disclosed in Table 1A or 1B. The second column provides the unique contig identifier, "Contig ID:" corresponding to contigs in Table 1B and allowing for correlation with the information in Table 1B. The third column provides the sequence identifier, "SEQ ID NO:X", for the contig polynucleotide sequence. The fourth column provides the analysis method by which the homology/identity disclosed in the Table was determined. Comparisons were made between polypeptides encoded by the polynucleotides of the invention and either a non-redundant protein database (herein referred to as "NR"), or a database of protein families (herein referred to as "PFAM") as further described below. The fifth column provides a description of the PFAM/NR hit having a significant match to a polypeptide of the invention. Column six provides the accession number of the PFAM/NR hit disclosed in the fifth column. Column seven, "Score/Percent Identity", provides a quality score or the percent identity, of the hit disclosed in columns five and six. Columns 8 and 9, "NT From" and "NT To" respectively, delineate the polynucleotides in "SEQ ID NO:X" that encode a polypeptide

having a significant match to the PFAM/NR database as disclosed in the fifth and sixth columns. In specific embodiments polypeptides of the invention comprise, or alternatively consist of, an amino acid sequence encoded by a polynucleotide in SEQ ID NO:X as delineated in columns 8 and 9, or fragments or variants thereof.

Description of Table 3

[54] Table 3 provides polynucleotide sequences that may be disclaimed according to certain embodiments of the invention. The first column provides a unique clone identifier, "Clone ID", for a cDNA clone related to contig sequences disclosed in Table 1B. The second column provides the sequence identifier, "SEQ ID NO:X", for contig sequences disclosed in Table 1A and/or 1B. The third column provides the unique contig identifier, "Contig ID:", for contigs disclosed in Table 1B. The fourth column provides a unique integer 'a' where 'a' is any integer between 1 and the final nucleotide minus 15 of SEQ ID NO:X, and the fifth column provides a unique integer 'b' where 'b' is any integer between 15 and the final nucleotide of SEQ ID NO:X, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:X, and where b is greater than or equal to a + 14. For each of the polynucleotides shown as SEQ ID NO:X, the uniquely defined integers can be substituted into the general formula of a-b, and used to describe polynucleotides which may be preferably excluded from the invention. In certain embodiments, preferably excluded from the invention are at least one, two, three, four, five, ten, or more of the polynucleotide sequence(s) having the accession number(s) disclosed in the sixth column of this Table (including for example, published sequence in connection with a particular BAC clone). In further embodiments, preferably excluded from the invention are the specific polynucleotide sequence(s) contained in the clones corresponding to at least one, two, three, four, five, ten, or more of the available material having the accession numbers identified in the sixth column of this Table (including for example, the actual sequence contained in an identified BAC clone).

Description of Table 4

[55] Table 4 provides a key to the tissue/cell source identifier code disclosed in Table 1B, column 8. Column 1 provides the tissue/cell source identifier code disclosed in Table 1B, Column 8. Columns 2-5 provide a description of the tissue or cell source. Codes corresponding to diseased tissues are indicated in column 6 with the word "disease". The use of the word "disease" in column 6 is non-limiting. The tissue or cell source may be

specific (e.g. a neoplasm), or may be disease-associated (e.g., a tissue sample from a normal portion of a diseased organ). Furthermore, tissues and/or cells lacking the "disease" designation may still be derived from sources directly or indirectly involved in a disease state or disorder, and therefore may have a further utility in that disease state or disorder. In numerous cases where the tissue/cell source is a library, column 7 identifies the vector used to generate the library.

Description of Table 5

[56] Table 5 provides a key to the OMIM reference identification numbers disclosed in Table 1B, column 10. OMIM reference identification numbers (Column 1) were derived from Online Mendelian Inheritance in Man (Online Mendelian Inheritance in Man, OMIM. McKusick-Nathans Institute for Genetic Medicine, Johns Hopkins University (Baltimore, MD) and National Center for Biotechnology Information, National Library of Medicine, (Bethesda, MD) 2000. World Wide Web URL: http://www.ncbi.nlm.nih.gov/omim/). Column 2 provides diseases associated with the cytologic band disclosed in Table 1B, column 9, as determined using the Morbid Map database.

Description of Table 6

[57] Table 6 summarizes some of the ATCC Deposits, Deposit dates, and ATCC designation numbers of deposits made with the ATCC in connection with the present application. These deposits were made in addition to those described in the Table 1A.

Description of Table 7

[58] Table 7 shows the cDNA libraries sequenced, and ATCC designation numbers and vector information relating to these cDNA libraries.

[59] The first column shows the first four letters indicating the Library from which each library clone was derived. The second column indicates the catalogued tissue description for the corresponding libraries. The third column indicates the vector containing the corresponding clones. The fourth column shows the ATCC deposit designation for each libray clone as indicated by the deposit information in Table 6.

Definitions

[60] The following definitions are provided to facilitate understanding of certain terms used throughout this specification.

[61] In the present invention, "isolated" refers to material removed from its original environment (e.g., the natural environment if it is naturally occurring), and thus is altered "by the hand of man" from its natural state. For example, an isolated polynucleotide could be part of a vector or a composition of matter, or could be contained within a cell, and still be "isolated" because that vector, composition of matter, or particular cell is not the original environment of the polynucleotide. The term "isolated" does not refer to genomic or cDNA libraries, whole cell total or mRNA preparations, genomic DNA preparations (including those separated by electrophoresis and transferred onto blots), sheared whole cell genomic DNA preparations or other compositions where the art demonstrates no distinguishing features of the polynucleotide/sequences of the present invention.

[62] In the present invention, a "secreted" protein refers to those proteins capable of being directed to the ER, secretory vesicles, or the extracellular space as a result of a signal sequence, as well as those proteins released into the extracellular space without necessarily containing a signal sequence. If the secreted protein is released into the extracellular space, the secreted protein can undergo extracellular processing to produce a "mature" protein. Release into the extracellular space can occur by many mechanisms, including exocytosis and proteolytic cleavage.

[63] As used herein, a "polynucleotide" refers to a molecule having a nucleic acid sequence encoding SEQ ID NO:Y or a fragment or variant thereof (e.g., the polypeptide delinated in columns fourteen and fifteen of Table 1A); a nucleic acid sequence contained in SEQ ID NO:X (as described in column 5 of Table 1A and/or column 3 of Table 1B) or the complement thereof; a cDNA sequence contained in Clone ID NO:Z (as described in column 2 of Table 1A and/or 1B and contained within a library deposited with the ATCC); a nucleotide sequence encoding the polypeptide encoded by a nucleotide sequence in SEQ ID NO:B as defined in column 6 (EXON From-To) of Table 1C or a fragment or variant thereof; or a nucleotide coding sequence in SEQ ID NO:B as defined

in column 6 of Table 1C or the complement thereof. For example, the polynucleotide can contain the nucleotide sequence of the full length cDNA sequence, including the 5' and 3' untranslated sequences, the coding region, as well as fragments, epitopes, domains, and variants of the nucleic acid sequence. Moreover, as used herein, a "polypeptide" refers to a molecule having an amino acid sequence encoded by a polynucleotide of the invention as broadly defined (obviously excluding poly-Phenylalanine or poly-Lysine peptide sequences which result from translation of a polyA tail of a sequence corresponding to a cDNA).

[64] In the present invention, "SEQ ID NO:X" was often generated by overlapping sequences contained in multiple clones (contig analysis). A representative clone containing all or most of the sequence for SEQ ID NO:X is deposited at Human Genome Sciences, Inc. (HGS) in a catalogued and archived library. As shown, for example, in column 2 of Table 1B, each clone is identified by a cDNA Clone ID (identifier generally referred to herein as Clone ID NO:Z). Each Clone ID is unique to an individual clone and the Clone ID is all the information needed to retrieve a given clone from the HGS library. Table 7 provides a list of the deposited cDNA libraries. One can use the Clone ID NO:Z to determine the library source by reference to Tables 6 and 7. Table 7 lists the deposited cDNA libraries by name and links each library to an ATCC Deposit. Library names contain four characters, for example, "HTWE." The name of a cDNA clone (Clone ID) isolated from that library begins with the same four characters, for example "HTWEP07". As mentioned below, Table 1A and/or 1B correlates the Clone ID names with SEQ ID NO:X. Thus, starting with an SEQ ID NO:X, one can use Tables 1A, 1B, 6, 7, and 9 to determine the corresponding Clone ID, which library it came from and which ATCC deposit the library is contained in. Furthermore, it is possible to retrieve a given cDNA clone from the source library by techniques known in the art and described elsewhere herein. The ATCC is located at 10801 University Boulevard, Manassas, Virginia 20110-2209, USA. The ATCC deposits were made pursuant to the terms of the Budapest Treaty on the international recognition of the deposit of microorganisms for the purposes of patent procedure.

[65] In specific embodiments, the polynucleotides of the invention are at least 15, at least 30, at least 50, at least 100, at least 125, at least 500, or at least 1000 continuous nucleotides but are less than or equal to 300 kb, 200 kb, 100 kb, 50 kb, 15 kb, 10 kb,

7.5kb, 5 kb, 2.5 kb, 2.0 kb, or 1 kb, in length. In a further embodiment, polynucleotides of the invention comprise a portion of the coding sequences, as disclosed herein, but do not comprise all or a portion of any intron. In another embodiment, the polynucleotides comprising coding sequences do not contain coding sequences of a genomic flanking gene (i.e., 5' or 3' to the gene of interest in the genome). In other embodiments, the polynucleotides of the invention do not contain the coding sequence of more than 1000, 500, 250, 100, 50, 25, 20, 15, 10, 5, 4, 3, 2, or 1 genomic flanking gene(s).

[66] A "polynucleotide" of the present invention also includes those polynucleotides capable of hybridizing, under stringent hybridization conditions, to sequences contained in SEQ ID NO:X, or the complement thereof (e.g., the complement of any one, two, three, four, or more of the polynucleotide fragments described herein), the polynucleotide sequence delineated in columns 7 and 8 of Table 1A or the complement thereof, the polynucleotide sequence delineated in columns 8 and 9 of Table 2 or the complement thereof, and/or cDNA sequences contained in Clone ID NO:Z (e.g., the complement of any one, two, three, four, or more of the polynucleotide fragments, or the cDNA clone within the pool of cDNA clones deposited with the ATCC, described herein), and/or the polynucleotide sequence delineated in column 6 of Table 1C or the complement thereof. "Stringent hybridization conditions" refers to an overnight incubation at 42 degree C in a solution comprising 50% formamide, 5x SSC (750 mM NaCl, 75 mM trisodium citrate), 50 mM sodium phosphate (pH 7.6), 5x Denhardt's solution, 10% dextran sulfate, and 20 μg/ml denatured, sheared salmon sperm DNA, followed by washing the filters in 0.1x SSC at about 65 degree C.

[67] Also contemplated are nucleic acid molecules that hybridize to the polynucleotides of the present invention at lower stringency hybridization conditions. Changes in the stringency of hybridization and signal detection are primarily accomplished through the manipulation of formamide concentration (lower percentages of formamide result in lowered stringency); salt conditions, or temperature. For example, lower stringency conditions include an overnight incubation at 37 degree C in a solution comprising 6X SSPE (20X SSPE = 3M NaCl; 0.2M NaH_2PO_4; 0.02M EDTA, pH 7.4), 0.5% SDS, 30% formamide, 100 ug/ml salmon sperm blocking DNA; followed by washes at 50 degree C with 1XSSPE, 0.1% SDS. In addition, to achieve even lower stringency,

washes performed following stringent hybridization can be done at higher salt concentrations (e.g. 5X SSC).

[68] Note that variations in the above conditions may be accomplished through the inclusion and/or substitution of alternate blocking reagents used to suppress background in hybridization experiments. Typical blocking reagents include Denhardt's reagent, BLOTTO, heparin, denatured salmon sperm DNA, and commercially available proprietary formulations. The inclusion of specific blocking reagents may require modification of the hybridization conditions described above, due to problems with compatibility.

[69] Of course, a polynucleotide which hybridizes only to polyA+ sequences (such as any 3' terminal polyA+ tract of a cDNA shown in the sequence listing), or to a complementary stretch of T (or U) residues, would not be included in the definition of "polynucleotide," since such a polynucleotide would hybridize to any nucleic acid molecule containing a poly (A) stretch or the complement thereof (e.g., practically any double-stranded cDNA clone generated using oligo dT as a primer).

[70] The polynucleotide of the present invention can be composed of any polyribonucleotide or polydeoxribonucleotide, which may be unmodified RNA or DNA or modified RNA or DNA. For example, polynucleotides can be composed of single- and double-stranded DNA, DNA that is a mixture of single- and double-stranded regions, single- and double-stranded RNA, and RNA that is mixture of single- and double-stranded regions, hybrid molecules comprising DNA and RNA that may be single-stranded or, more typically, double-stranded or a mixture of single- and double-stranded regions. In addition, the polynucleotide can be composed of triple-stranded regions comprising RNA or DNA or both RNA and DNA. A polynucleotide may also contain one or more modified bases or DNA or RNA backbones modified for stability or for other reasons. "Modified" bases include, for example, tritylated bases and unusual bases such as inosine. A variety of modifications can be made to DNA and RNA; thus, "polynucleotide" embraces chemically, enzymatically, or metabolically modified forms.

[71] In specific embodiments, the polynucleotides of the invention are at least 15, at least 30, at least 50, at least 100, at least 125, at least 500, or at least 1000 continuous

nucleotides but are less than or equal to 300 kb, 200 kb, 100 kb, 50 kb, 15 kb, 10 kb, 7.5kb, 5 kb, 2.5 kb, 2.0 kb, or 1 kb, in length. In a further embodiment, polynucleotides of the invention comprise a portion of the coding sequences, as disclosed herein, but do not comprise all or a portion of any intron. In another embodiment, the polynucleotides comprising coding sequences do not contain coding sequences of a genomic flanking gene (i.e., 5' or 3' to the gene of interest in the genome). In other embodiments, the polynucleotides of the invention do not contain the coding sequence of more than 1000, 500, 250, 100, 50, 25, 20, 15, 10, 5, 4, 3, 2, or 1 genomic flanking gene(s).

[72] "SEQ ID NO:X" refers to a polynucleotide sequence described in column 5 of Table 1A, while "SEQ ID NO:Y" refers to a polypeptide sequence described in column 10 of Table 1A. SEQ ID NO:X is identified by an integer specified in column 6 of Table 1A. The polypeptide sequence SEQ ID NO:Y is a translated open reading frame (ORF) encoded by polynucleotide SEQ ID NO:X. The polynucleotide sequences are shown in the sequence listing immediately followed by all of the polypeptide sequences. Thus, a polypeptide sequence corresponding to polynucleotide sequence SEQ ID NO:2 is the first polypeptide sequence shown in the sequence listing. The second polypeptide sequence corresponds to the polynucleotide sequence shown as SEQ ID NO:3, and so on.

[73] The polypeptide of the present invention can be composed of amino acids joined to each other by peptide bonds or modified peptide bonds, i.e., peptide isosteres, and may contain amino acids other than the 20 gene-encoded amino acids. The polypeptides may be modified by either natural processes, such as posttranslational processing, or by chemical modification techniques which are well known in the art. Such modifications are well described in basic texts and in more detailed monographs, as well as in a voluminous research literature. Modifications can occur anywhere in a polypeptide, including the peptide backbone, the amino acid side-chains and the amino or carboxyl termini. It will be appreciated that the same type of modification may be present in the same or varying degrees at several sites in a given polypeptide. Also, a given polypeptide may contain many types of modifications. Polypeptides may be branched, for example, as a result of ubiquitination, and they may be cyclic, with or without branching. Cyclic, branched, and branched cyclic polypeptides may result from posttranslation natural processes or may be made by synthetic methods. Modifications include acetylation, acylation, ADP-ribosylation, amidation, covalent attachment of flavin,

covalent attachment of a heme moiety, covalent attachment of a nucleotide or nucleotide derivative, covalent attachment of a lipid or lipid derivative, covalent attachment of phosphotidylinositol, cross-linking, cyclization, disulfide bond formation, demethylation, formation of covalent cross-links, formation of cysteine, formation of pyroglutamate, formylation, gamma-carboxylation, glycosylation, GPI anchor formation, hydroxylation, iodination, methylation, myristoylation, oxidation, pegylation, proteolytic processing, phosphorylation, prenylation, racemization, selenoylation, sulfation, transfer-RNA mediated addition of amino acids to proteins such as arginylation, and ubiquitination. (See, for instance, PROTEINS - STRUCTURE AND MOLECULAR PROPERTIES, 2nd Ed., T. E. Creighton, W. H. Freeman and Company, New York (1993); POSTTRANSLATIONAL COVALENT MODIFICATION OF PROTEINS, B. C. Johnson, Ed., Academic Press, New York, pgs. 1-12 (1983); Seifter et al., Meth. Enzymol. 182:626-646 (1990); Rattan et al., Ann. N.Y. Acad. Sci. 663:48-62 (1992)).

[74] "SEQ ID NO:X" refers to a polynucleotide sequence described, for example, in Tables 1A, 1B or 2, while "SEQ ID NO:Y" refers to a polypeptide sequence described in column 11 of Table 1A and or column 6 of Table 1B. SEQ ID NO:X is identified by an integer specified in column 4 of Table 1B. The polypeptide sequence SEQ ID NO:Y is a translated open reading frame (ORF) encoded by polynucleotide SEQ ID NO:X. "Clone ID NO:Z" refers to a cDNA clone described in column 2 of Table 1A and/or 1B.

[75] "A polypeptide having functional activity" refers to a polypeptide capable of displaying one or more known functional activities associated with a full-length (complete) protein. Such functional activities include, but are not limited to, biological activity, antigenicity [ability to bind (or compete with a polypeptide for binding) to an anti-polypeptide antibody], immunogenicity (ability to generate antibody which binds to a specific polypeptide of the invention), ability to form multimers with polypeptides of the invention, and ability to bind to a receptor or ligand for a polypeptide.

[76] The polypeptides of the invention can be assayed for functional activity (e.g. biological activity) using or routinely modifying assays known in the art, as well as assays described herein. Specifically, one of skill in the art may routinely assay secreted polypeptides (including fragments and variants) of the invention for activity using assays as described in the examples section below.

[77] "A polypeptide having biological activity" refers to a polypeptide exhibiting activity similar to, but not necessarily identical to, an activity of a polypeptide of the present invention, including mature forms, as measured in a particular biological assay, with or without dose dependency. In the case where dose dependency does exist, it need not be identical to that of the polypeptide, but rather substantially similar to the dose-dependence in a given activity as compared to the polypeptide of the present invention (i.e., the candidate polypeptide will exhibit greater activity or not more than about 25-fold less and, preferably, not more than about tenfold less activity, and most preferably, not more than about three-fold less activity relative to the polypeptide of the present invention).